UROLOGIC ASPECTS OF HYPERPARATHYROIDISM*

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WITHIN four decades, primary hyperparathyroidism has evolved from a clinical curiosity to a common endocrinopathy with a broad spectrum of clinical manifestations and associated diseases. Renal involvement is a serious and by far the most common deleterious effect of excess of parathyroid hormone. An estimated 2 to 10% of those who form stones have been found to have hyperparathyroidism.[1]

EXPERIMENTAL BACKGROUND

In various animals, experimental intoxication with parathyroid hormone produces morphologic changes closely resembling those of clinical hyperparathyroidism in man. The pathologic changes which are common to all consist of mitochondrial damage and accumulation of high-molecular-weight periodic acid-Schiff-positive mucosubstances within the cytoplasm and lumen of the tubules.[2] Subsequent mineralization by microcrystals (35 by 250 A) of hydroxyapatite is followed by extrusion of the calcified microlith into the lumen of the nephron, where further deposition of calcium-containing crystals may occur.[1, 2] Some of these intranephronic calculi may cause tubular blockage, resulting in death of the nephron with secondary amorphous accumulations about the concretion and below it.[2] Other calculi may migrate into a submucosal or intralymphatic position, and thus represent Randall's plaques or Carr's bodies.[3]

Among the more advanced cases, pathologic calcifications of the necrotic tubular epithelium, its basement membrane, and adjacent interstitial tissues, particularly marked in the distal nephron, are the most striking features. Secondary changes caused by urinary infection or obstruction may supervene and later dominate the picture.[1]

CLINICAL DATA

Of 401 patients with disorders of calcium metabolism investigated at the Mayo Clinic during a two-and-one-half-year period, 171 had surgically proved primary hyperparathyroidism.[4] Their ages ranged from 10 to 89 years. Women were affected twice as frequently as men.

Urologic complications were noted in 59% of these patients and included nephrolithiasis (46%), nephrocalcinosis (5%), and significant impairment of renal function (8%). The relatively low incidence of nephrocalcinosis—which was accompanied by nephrolithiasis in every instance—in this series may be partly related to the fact that calcifications in the tubules near papillary tips were not included.

Renal lithiasis was the most common complication. However, metabolically active stone disease, as judged by documented additional or new stone formation or passage of gravel within the year prior to parathyroidectomy, was present in only 10.5% of the patients.

Calculi were more commonly unilateral and in all but three instances contained calcium without producing any distinguishing roentgenographic appearances; the three instances were rare examples of pure uric acid lithiasis occurring as a manifestation of hyperparathyroidism and responded to treatment of the endocrinopathy.

Contrary to data presented by Lloyd,[5] stone disease and bone disease did not seem to represent separate clinical entities. Indeed, 68% of 41 patients with roentgenographic evidence of bone disease also had renal calculi. In nine of the 14 patients with significant renal impairment, despite measures to prevent postoperative oliguria, further deterioration of function followed parathyroid adenectomy; fortunately, all regained their preoperative renal function three months later. In the five other patients, actual improvement occurred postoperatively.

DISCUSSION

The formation of stones occurred in only one half of this group of 171 patients; there were no significant differences in clinical and biochemical data between patients with active stone disease and those with other classifications of stone disease or without stone disease. This illustrates the complexity and multiplicity, as well as our ignorance, of the factors involved in lithogenesis.

The exact nature of and reasons for the earliest and reversible changes in renal function, manifested by tubular inability to concentrate and

acidify urine, are poorly understood. More advanced functional impairment accompanied by histologic evidence of renal parenchymal damage, reflected in diminished renal plasma flow and glomerular filtration rate, has been reported in a significant proportion of patients.[1] The most severe and irreversible changes have occurred more frequently in patients with advanced bone disease or nephrocalcinosis. Relief of the calculous obstruction and treatment of the urinary infection obviously would help to normalize renal function.

In general, parathyroidectomy should be carried out before treatment of the calculous disease is undertaken. The reverse order is fraught with dangers of postoperative hypercalcemic crisis and rapid recurrence of calculous material.

Management of urolithiasis depends upon the type of activity of the stone disease. We have arbitrarily classified the activity of stone disease in the following manner:

Metabolically active, indicating that one or more of the following has occurred: 1) the formation of new stones in the past year, 2) the growth of an existing stone in the past year, and 3) the documented passage of gravel in the past year.

Metabolically inactive, indicating that none of the above has occurred—that is, no change in the formation of stones in the past year.

Indeterminate activity, when available data are inadequate for classification.

Surgical activity, when the stone-bearing kidney becomes obstructed, infected, painful, or hemorrhagic; surgical intervention then becomes necessary.

Surgically active or infected calculi should be removed. Patients with metabolically inactive, indeterminate, or active but uninfected renal lithiasis rendered inactive by parathyroidectomy should be watched carefully. The subsequent development of urosepsis, the growth of stone, or surgical activity may necessitate surgical intervention. Infrequently, control of metabolically active stone disease after parathyroidectomy requires phosphate therapy.

Complicated situations such as the coexistence of tumors producing parathyroid hormone-like substances and primary hyperparathyroidism tax the judgment of most clinicians. An increase in serum immunoreactive parathyroid hormone (iPTH) that shows a positive correlation with the degree of hypercalcemia appears to be produced specifical-

ly by the hyperfunctioning parathyroid gland. In our limited experience, this correlation serves as a useful aid in differentiating this entity from the hypercalcemia of malignancy.[4] Exceptionally, a substance resembling parathyroid hormone and produced by renal cell carcinomas seems to have immunoreactive characteristics identical to those of true parathyroid hormone. At present the actual cause of hypercalcemia occurring under such circumstances may be determined only in a stepwise fashion by elimination and careful reevaluation.

CONCLUSION

Hyperparathyroidism is a disease of astonishing variety, both in severity and in mode of clinical expression. Early treatment of this disorder is the most important step. As urologists, we can help to reduce the large number of mistreated renal invalids only if we develop an awareness of this condition in differential diagnosis.

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